NEUTRALIZING ANTI-SARS-COV-2 ANTIBODIES AND METHODS OF USE THEREOF

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority under 35 U.S.C. § 119(e) to U.S. Provisional Patent Application No. 63/016,569, filed Apr. 28, 2020, to U.S. Provisional Patent Application No. 63/021,387, filed May 7, 2020, to U.S. Provisional Patent Application No. 63/032,112, filed May 29, 2020, to U.S. Provisional Patent Application No. 63/038,384, filed Jun. 12, 2020, and to U.S. Provisional Patent Application No. 63/119,088, filed Nov. 30, 2020. The foregoing applications are incorporated by reference herein in their entireties.

STATEMENT REGARDING FEDERALLY FUNDED RESEARCH

[0002] This invention was made with government support under grant nos. P01-AI138398-S1 and 2U19AI111825 awarded by the National Institutes of Health. The government has certain rights in the invention.

SEQUENCE LISTING

[0003] The instant application contains a Sequence Listing which has been submitted electronically in ASCII format and is hereby incorporated by reference in its entirety. Said ASCII copy, created on Jun. 8, 2021, is named 070413_20615_SL.txt and is 3,009,383 bytes in size.

FIELD OF THE INVENTION

[0004] The present invention relates to antibodies directed to epitopes of SARS-CoV-2 Coronavirus 2 ("SARS-CoV-2"). The present invention further relates to the preparation and use of broadly neutralizing antibodies directed to the SARS-CoV-2 spike (S) glycoproteins for the prevention and treatment of SARS-CoV-2 infection.

BACKGROUND OF THE INVENTION

[0005] SARS-CoV-2 is the virus that causes coronavirus disease 2019 (COVID-19). It contains four structural proteins, including spike (S), envelope (E), membrane (M), and nucleocapsid (N) proteins. Among them, S protein plays the most important roles in viral attachment, fusion, and entry, and it serves as a target for development of antibodies, entry inhibitors, and vaccines. The S protein mediates viral entry into host cells by first binding to a host receptor through the receptor-binding domain (RBD) in the S1 subunit and then fusing the viral and host membranes through the S2 subunit. SARS-CoV and MERS-CoV RBDs recognize different receptors. SARS-CoV recognizes angiotensin-converting enzyme 2 (ACE2) as its receptor, whereas MERS-CoV recognizes dipeptidyl peptidase 4 (DPP4) as its receptor. Similar to SARS-CoV, SARS-CoV-2 also recognizes ACE2 as its host receptor binding to viral S protein.

[0006] As of Apr. 25, 2020, a total of 2.84 million confirmed cases of COVID-19 were reported, including 199,000 deaths, in the United States and at least 85 other countries and/or territories. Currently, the intermediate host of SARS-CoV-2 is still unknown, and no effective prophylactics or therapeutics are available. This calls for the immediate development of vaccines and antiviral drugs for prevention and treatment of COVID-19.

[0007] In addition, due to the ability of SARS-CoV-2 to be spread through an airborne route, SARS-CoV-2 presents a particular threat to the health of large populations of people throughout the world. Accordingly, methods to immunize people before infection, diagnose infection, immunize people during infection, and treat infected persons infected with SARS-CoV-2 are urgently needed.

SUMMARY OF THE INVENTION

[0008] This disclosure addresses the need mentioned above in a number of aspects by providing broadly neutralizing anti-SARS-CoV-2 antibodies or antigen-binding fragments thereof.

[0009] In one aspect, this disclosure provides an isolated anti-SARS-CoV-2 antibody or antigen-binding fragment thereof that binds specifically to a SARS-CoV-2 antigen. In some embodiments, the SARS-CoV-2 antigen comprises a Spike (S) polypeptide, such as a S polypeptide of a human or an animal SARS-CoV-2. In some embodiments, the SARS-CoV-2 antigen comprises the receptor-binding domain (RBD) of the S polypeptide. In some embodiments, the RBD comprises amino acids 319-541 of the S polypeptide.

[0010] In some embodiments, the antibody or antigen-binding fragment thereof is capable of neutralizing a plurality of SARS-CoV-2 strains.

[0011] In some embodiments, the antibody or antigen-binding fragment thereof comprises three heavy chain complementarity determining regions (HCDRs) (HCDR1, HCDR2, and HCDR3) of a heavy chain variable region having an amino acid sequence of SEQ ID NOs: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 2876, or 2900; and three light chain CDRs (LCDR1, LCDR2, and LCDR3) of a light chain variable region having the amino acid sequence of SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 2888, or 2912.

[0012] In some embodiments, HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 comprise respective amino acid sequences of (i) SEQ ID NOs: 2878, 2880, 2882, 2890, 2892, and 2894; or (ii) SEQ ID NOs: 2902, 2904, 2906, 2914, 2916, and 2918.

[0013] In some embodiments, the antibody or antigen-binding fragment thereof comprises: (i) a heavy chain variable region having an amino acid sequence with at least 75% identity to SEQ ID NOs: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137,